REMARKS

The Office Action mailed January 30, 2002 has been received and reviewed. Claims 1, 4-12, 15-17, 19, 21-24, 47 and 71-73 are currently pending in the application. Claims 10, 19, 47 and 73 are withdrawn from consideration as being subject to restriction. Claims 1, 4-9, 11, 12, 15-17, 21-24, 71 and 72 stand rejected. Applicants have amended claims 1, 6, 8, 12, 15-17, 21-23 and 71, cancelled claims 7 and 24, and added new claims 74-87 as set forth herein. All amendments and cancellations are made without prejudice or disclaimer. Reconsideration is respectfully requested.

Restriction

Applicants note the traversal of the restriction requirement in the Amendment filed November 8, 2001.

Specification

Title

The title of the invention was deemed not descriptive because it was thought that "the instant invention is directed to peptides with antagonist activity against IL-6 and not peptides with agonist activity." (Office Action mailed January 30, 2002, page 3). The current title is descriptive since a peptide derived from SEQ ID NO: 11 in the present invention displays agonistic activity. As stated in the specification, "[a]gonistic activity was observed in a concentration range from 7.5 to 120 µg/ml peptide." (Specification, page 15, lines 29-30.) Since the present title is descriptive of the present invention, reconsideration of the objection is requested.

Brief Description of Figures

The specification was objected to because it failed to provide a brief description of Figures. Applicants have amended the specification to include a paragraph reciting a brief description of Figures. Withdrawal of the objection is thus requested.

Objections to Claims

Claim 6

Claim 6 was objected to because it recites SEQ ID NOs not currently elected for examination. Although applicants do not agree with the restriction requirement, to expedite prosecution of the present application, claim 6 has been amended to be directed to SEQ ID NO: 5. Reconsideration is respectfully requested.

Claim 8

Claim 8 was objected to because of the presence of the recitation "any of claim 1," when the claim could only depend from claim 1. Claim 8 has been amended to recite "according to claim 1." Reconsideration is requested.

Claims 11 and 72

Claims 11 and 72 were objected to for assertedly claiming the same subject matter. Claims 11 and 72 are not directed to identical subject matter. Claim 11 is directed to a peptide composition wherein at least two peptides according to claim 1 are chemically linked directly or via spacer molecules. Claim 11 also requires that at least four peptides are linked with branching oligolysines.

Claim 72 is directed to a peptide composition wherein at least two peptides according to claim 1 are chemically linked directly or via spacer molecules, wherein the at least two peptides are linked with lysine. Claim 72 further requires that at least four peptides be linked with branching oligolysines. Since claim 72 depends from claim 9, claim 72 requires a limitation not required by claim 11. Accordingly, reconsideration is requested.

Rejections under 35 U.S.C. § 101

Claims 17, 21 and 24

Claims 17, 21 and 24 were rejected under 35 U.S.C. § 101 because they claimed recitation of a use without setting forth any steps involved in the process, resulting in an improper definition of a process. Claims 17 and 21 have been amended, and in view of the amendments, applicants respectfully traverse the rejections. Claim 24 has been cancelled making the rejection of claim 24 moot.

Claim 17 has been amended to recite in part "a method of treating or preventing an IL-6 related disease." Claim 21 has also been amended to recite "[a] method for culturing cells comprising contacting said cells, or medium wherein said cells are cultured with a peptide according to claim 1." Since the amended claims set forth steps in a process, reconsideration and withdrawal of the rejections are requested.

Claim 1

Claim 1 was rejected under 35 U.S.C. § 101 because the phrase "A peptide" was deemed to read on a product of nature, and failed to indicate the hand of man in the invention. Claim 1 has been amended and in view thereof, applicants respectfully traverse the rejection.

As amended, claim 1 is directed to "an isolated, recombinant or purified peptide." Reconsideration and withdrawal of the rejection of claim 1 are thus requested.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 4-9, 11-12, 15-17, 21-24 and 71-72 were rejected under 35 U.S.C. § 112, first paragraph, because the specification was thought to lack enablement to provide any person skilled in the art to make the invention commensurate in scope with the claims. Applicants have amended claims 1, 6, 8, 12, 15-17, 21-23 and 71, and in view of the amendments respectfully traverse the rejections. Claims 7 and 24 have been cancelled making the rejections of these claims moot.

The Office Action asserted that "the specification, while being enabling for a peptide of 5-30 amino acids, or 5-20 amino acids of SEQ ID No. 5 and SEQ ID No. 11 which peptides exhibit antagonistic or agonistic activity directed against IL-6 respectively... does not reasonably provide enablement for 'any other' peptides of 5-30 amino acids, or 5-20 amino acids." (Office Action, page 5). However, the application provides sufficient guidance for a person skilled in the art to ascertain whether a certain peptide, or linked peptide, exhibits antagonistic activity against IL-6. For instance, the specification discloses a proliferation assay to determine antagonistic IL-6 activity. (*See*, Specification, page 10, line 16 through page 12, line 2). Also, the specification describes how a candidate IL-6 antagonistic peptide can be tested by determining its effect upon IL-6 induced phase reaction and downregulation of hepatic biotransformation activities. (*See*, *Id.*, page 13, line 6 through page 14, line 32)

The Office Action also states that "the guidance provided is insufficient to for one of skill in the art to test whether SEQ ID NO. 5, and SEQ ID NO. 11 would be expected to have what type of functionality as recited in the instant claims." (Office Action, page 6). However, the specification does show the functionality recited in the claims because antagonistic or agonistic activity of a peptide of the invention, *i.e.*, a peptide comprising at least one string of 5 consecutive amino acids long in common with SEQ ID NO: 11, is demonstrated as depending on the concentration of the peptide involved. (*See*, Specification, page 15, lines 29-37). For instance, agonistic activity was observed in a range from 7.5 to 120 μg/ml peptide, while at a concentration over 120 μg/ml peptide, the peptide had an antagonistic effect. (*See*, *Id.*) Using the teachings of the present invention, a person skilled in the art would be able to test candidate peptides for the claimed function, antagonistic activity directed against IL-6. (*See*, *Id.*)

Claims 1, 4-9, 11-12, 15-17, 21-24 and 71-72 were also rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventors has possession of

the claimed invention. Claims 7 and 24 have been cancelled making the rejections of these claims moot. In view of the amendments to claims 1, 6, 8, 12, 15-17, 21-23 and 71, applicants respectfully traverse the rejections.

Specifically, the Office Action states "the written description sets forth at least 5 consecutive amino acids of SEQ ID No. 11 to have agonistic activity [], while at least 5 consecutive amino acids of SEQ ID NO. 5 to have antagonistic activity." (Office Action, page 8). The peptides of the present invention may exhibit both agonistic and antagonistic activity, depending on the concentration of the peptide. The specification indicates that "[a]gonistic activity was observed in a concentration range from 7.5 to 120 μg/ml peptide[, while] at a concentration of $\geq$ 120 μg/ml these agonistic peptides had an antagonistic effect upon the biological activity of IL-6." (Specification, page 15, lines 29-37). Therefore, the applicants are in possession of the invention as claimed.

Even though applicants disagree with the assertions in the Office Action that the specification is non-enabling, to expedite prosecution of the application, claims 1, 6, 8, 12, 15-17, 21-23 and 71 have been amended. Accordingly, reconsideration and withdrawal of the rejections of claims 1, 4-6, 8, 9, 11-12, 15-17, 21-23 and 71-72 are requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1, 4-9, 11-12, 15-17, 21-24 and 71-72 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as their invention. Applicants have amended claims 1, 6, 8, 12, 15-17, 21-23 and 71, and in view of the amendments respectfully traverse the rejections. Claims 7 and 24 have been cancelled rendering the rejections of these claims moot.

Specifically, claim 1 was rejected as being indefinite for reading on a product of nature. Claim 1 has been amended in accordance with the Examiner's suggestions.

Claims 12 and 15-17 were rejected as being indefinite for lacking antecedent basis for "peptide compositions." The claims have been amended to provide antecedent basis. Further, new claims 74-83 have been added to avoid multiple dependencies and to provide antecedent basis for "an antibody."

With further regard to claim 16, it was rejected for lacking the method steps required to use the instant IL-6 antagonists for the intended purpose. Claim 16 has been amended to include a method step.

Claims 16 and 17 were also rejected because it was not clear why a skilled artisan would use "a method for clearing... blood products ... using IL-6 antagonists." (Office Action, page 9). The method of claim 16 may be used to remove circulating IL-6 from the blood of a diseased

patient. (*See*, Specification, page 8, lines 23-31.) Also, claim 17 has been amended to recite "a method for treating or preventing an IL-6 related disease."

With regard to claim 21, it was rejected as depending from cancelled claim 20. Claim 21 has been amended to recite a method claim depending from claim 1.

Claim 23 was rejected as assertedly being indefinite for reciting a "peptide composition" with no antecedent basis in claim 1 from which it depends and for lacking method steps. (Office Action, page 9). Claim 23 was also rejected as being vague and indefinite because it was asserted that the phrase "intra-mammary application" was not clear. (*Id.* at page 10). As amended, claim 1 provides antecedent basis for claim 23. Claim 23 has also been amended for the sake of clarity to include a method step. Further, since methods for manufacturing medicaments and intra-mammary applications are well known by those of ordinary skill in the art, claim 23 is definite.

Claims 17, 21 and 24 were rejected as being indefinite for reciting the phrase "use for." (*Id.*) Claims 17 and 21 have been amended to include method steps.

Claims 4-9, 11 and 22 were rejected as depending from indefinite independent claim 1. Claim 1 has been amended and accordingly, is definite. Therefore, claims 4-6, 8 and 9 are definite as depending from a definite base claim.

In light of the amendments to claims 1, 6, 8, 12, 15-17, 21-23 and 71 and the remarks presented herein, the claims are definite. Accordingly, reconsideration and withdrawal of the indefiniteness rejections of claims 1, 4-6, 8, 9, 11-12, 15-17, 21-23 and 71-72 are requested.

Rejections under 35 U.S.C. § 102

Claims 1, 4-5, 7, 15-17, 21-24 and 71 were rejected under 35 U.S.C. § 102(b) as being anticipated by EP 0426857 (5/15/1991) and U.S. Patent 5,210,075 (05/1993). Claims 1, 15-17, 21-24 and 71 have been amended and in view of the amendments, applicants respectfully traverse the rejections as hereinafter set forth. Claims 7 and 24 have been cancelled rendering the anticipation rejections of these claims moot.

Claim 1 has been amended to require the peptide of SEQ ID NO: 11. Since neither EP 0426857 nor U.S. Patent 5,210,075 disclose the peptide having at least one string of 5 consecutive amino acids long in common with SEQ ID NO: 11, the cited references do not anticipate claim 1. Since claim 4-5, 15-17, 21-23 and 71 depend, directly or indirectly, from novel independent claim 1, they are also not anticipated. Therefore, reconsideration and withdrawal of the anticipation rejections of the claims are requested.

CONCLUSION

If questions exist after consideration of the foregoing, the Office is kindly requested to contact the applicants' representative at the address or telephone number below.

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AFN
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Attachments: Marked up Version of Claims

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MARKED UP VERSION OF CLAIMS

1. (Amended) [A] An isolated, recombinant or purified peptide of 5-30 amino acids which peptide exhibits antagonistic activity directed against IL-6, having at least one string of 5 consecutive amino acids long in common with the following amino acid sequence: EWGPRSTPSLTTKAVLLLVRKFQNSPAED (SEQ ID NO: 11).

5. (Amended) [A] The isolated, recombinant or purified peptide [according to] of claim [4] 1 of 5-12 amino acids.

6. (Thrice Amended) [A] The isolated, recombinant or purified peptide [according to] of claim 1 having at least one string of 5 consecutive amino acids long in common with [one of] the following amino acid [sequences] sequence: [STKVLIQFLQKKAKNL (SEQ. ID. NO.: 2), ILRSFKEFLQSSLRALRQM (SEQ. ID. NO.: 3), QLSCFRKSPLSNVVC (SEQ. ID. NO.: 4),] PRSTPSLTTKAVLLLVRKFQNS (SEQ[.] ID[.] NO[.]: 5)[, MCVASSVGSKFSKTQTFQGC (SEQ. ID. NO.: 6), PEKPKNLSCIVNEGKKMRCEWDGGR (SEQ. ID. NO.: 7), NFTLKSEQATHKFADCKAKRDTPTS (SEQ. ID. NO.: 8), WVEAENALGKVTSDH (SEQ. ID. NO.: 9), or PVYKVKPNPPHNLSVIN (SEQ. ID. NO.: 10)].

8. (Amended) A peptide composition, wherein at least two isolated, recombinant or purified peptides [according to any] of claim 1 are chemically linked directly or via spacer molecules.

12. (Amended) A mixture comprising the isolated, recombinant or purified peptides [and/or peptide composition according to] of claim 1.

15. (Amended) A pharmaceutical preparation comprising [a] the isolated, recombinant or purified peptide [or a peptide composition or an antibody according to] of claim 1, together with at least one suitable excipient for administration.

16. (Twice Amended) A method for clearing extra-corporeal blood or blood products from IL-6 or IL-6 receptor molecules [using] comprising contacting said blood or blood product with [a] the isolated, recombinant or purified peptide [, peptide composition or antibody] of claim 1.

17. (Amended) [Use of a peptide, peptide composition or antibody] A method for treating or preventing an IL-6 related disease using the pharmaceutical preparation [according to] of claim [1] 15 [to clear extra-corporeal blood or blood products from IL-6 or IL-6 receptor antagonists].

21. (Amended) [Use of] A method for culturing cells comprising contacting said cells, or medium wherein said cells are cultured, with [a] the isolated, recombinant or purified peptide [according to] of claim [20] 1 [in cell culture].

22. (Amended) A pharmaceutical preparation comprising [a] the isolated, recombinant or purified peptide [according to] of claim [7] 6 together with at least one suitable excipient for administration.

23. (Twice Amended) A method for manufacturing a medicament [comprising a peptide, or peptide combination] for topical or intra-mammary application, characterized in that the isolated, recombinant or purified peptide [according to] of claim 1 is used.

71. (Amended) The isolated, recombinant or purified peptide of claim 5 having at least one string of 5 consecutive amino acids long in common with the following amino acid sequence: [EWGPRSTPSLTTKAVLLLVRKFQNSPAED (SEQ ID NO: 11)] PRSTPSLTTKAVLLLVRKFQNS (SEQ ID NO: 5).